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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	10

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/550,163	ABBOTT ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-68* is/are pending in the application.

4a) Of the above claim(s) *10-23 and 31-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It was not executed in accordance with either 37 CFR 1.66 or 1.68.

Mark T. Keating signed his name, but did write down the date he signed

Priority

This application claims benefit of 60/129,404 filed on 15 April 1999 is acknowledged.

In response to the election/restriction (paper no.8, 20 June 2001), applicants elect the claims of Group I (claims 1-9 and 24-30) as drawn to a nucleic acid encoding the protein of SEQ ID NO: 2 is acknowledged.

Thus, claims 10-23, 31-68, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 9.

Elected claims 1-9 and 24-30, to which the following grounds of rejection are applicable, are pending examination.

Claim Objections

Claims 1, 4, 5, 6, 7, 25, 27, and 29 are objected to because the claims still read on non-elected embodiment (*e.g.* SEQ ID NO: 4, 6, 8, 10, and 12).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2, as best understood, is readable on a genus of an isolated DNA encoding a polypeptide of SEQ ID NO: 2 comprising a mutation disclosed herein is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5, 7, and 8, as best understood, are readable on a genus of an allelic variant of the DNA of claim 1 and/or an allelic variant of SEQ ID NO: 2 are not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 9, as best understood, is readable on a genus of a polymorphic site which is used for performing a single base extension primer across a subsequence of SEQ ID NO: 2 is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as

containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates production of a species of isolated DNA encoding a polypeptide of SEQ ID NO: 2 comprising a mutation disclosed herein; an allelic variant of a DNA sequence in claim and/or allelic variant of amino acid sequence set forth in SEQ ID NO: 2, and a polymorphic site. The as-filed specification provides sufficient description of a species of an isolated DNA coding human MiRP1 in SEQ ID NO: 1. Furthermore, the as-filed specification further provides description of a species of SEQ ID NO: 1 comprising a Q9E, M54T, I57T, and T8A mutation in the sequence (pages 72-73). However, the as-filed specification does not provide sufficient description of a polymorphic site which can used for performing a single base extension reaction across a subsequence of SEQ ID NO: 2 or the complement thereof. In addition, the as-filed specification does not provide sufficient description of an allelic variant that hybridizes to SEQ ID NO: 1; shares 90% identity to SEQ ID NO: 1, or is a mutation of an isolated DNA encoding a polypeptide of SEQ ID NO: 2.

However, it is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of allelic variants of any nucleotide sequence which hybridizes to SEQ ID NO: 1 and/or a polymorphic site in a subsequence of SEQ ID: 2 and/or an isolated mutated DNA sequence of SEQ ID NO: 2; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or

molecular structures of polymorphic sites, allelic variants, and/or mutated nucleic acids sequences encoding SEQ ID NO: 2 that must exhibit the disclosed biological functions as contemplated by the claims.

It is not sufficient to support the present claimed invention directed to a genus of isolated DNA encoding a polypeptide of SEQ ID NO: 2 comprising a mutation disclosed herein; an allelic variant of a DNA sequence in claim and/or allelic variant of amino acid sequence set forth in SEQ ID NO: 2, and a polymorphic site which can used in a single base extension reaction across a subsequence of SEQ ID NO: 2. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming unspecified polymorphic sites and/or a genus of an amino acid sequences and/or DNA sequences that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of the claimed polymorphic site; DNA sequences and/or amino acid sequences that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to

practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-9 and 24-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a nucleic acid comprising a nucleotide sequence coding for human MiRP1 set forth in SEQ ID NO: 2 or the complement of SEQ ID NO: 1; 2) An in vitro cell transfected with the DNA of SEQ ID NO: 2; 3) A vector comprising the isolated DNA of SEQ ID NO: 2; 4) An in vitro cell transfected with the vector of 4; 5) An isolated nucleic acid comprising of at least 10 consecutive nucleotide residues of SEQ ID NO: 1 6) An isolated nucleic acid consisting of a mutated human MiRP1 (SEQ ID NO:1) selected from the group consisting of one of the following mutant human MiRP1 genes: a) Q9E-hMiRP1, b) M54T-hMiRP1, c) I57T-hMiRP1, or d) T8A-hMiRP1. The specification does not reasonably provide enablement for any other embodiment as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of a genus of allelic variants of DNA sequences and/or amino acid sequence of SEQ ID NO: 1 and 2, respectively; polymorphic sites in SEQ ID NO: 2), particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended.

The disclosure also claims using nucleotide sequences, which hybridizes under stringent conditions to the nucleotide sequence encoding SEQ ID NO: 2 or its complement or any fragment thereof. In view of the state of the art and the as-filed specification, it is not apparent to one skilled in the art if any of the nucleic acid sequences with a mutation or at least 90% identity with nucleic acid encoding SEQ ID NO: 2, which hybridizes under any stringent condition would possess the same biological activity compared to the wild-type MiRP1. In addition, it is not apparent to one skilled in the art how the nucleic acid sequences complementary to the nucleotide sequence encoding SEQ ID NOs: 2 exhibit biological activity as contemplated by the specification. Since, the relationship between a sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Chiu et al., *Folding and Design*, 1998, pp. 23-228), it would required undue experimentation for one skilled in the art to arrive at other peptides that have MiRP1 activity. In addition, in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 U.S.C. 112, first paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required

of one skilled in the art for the determination of other genetic sequences that are embraced by the claim. This is the case here. In other words, since it would require undue experimentation to identify other peptides that have MiRP1 activity, it certainty would require undue experimentation to make their corresponding DNA and, therefore any other nucleotide sequence other than the MiRP1 encoded by SEQ ID NO: 1 is not enabled by the specification.

With respect to claims encompassing using a nucleic acid probe which hybridizes specifically to the nucleotide sequence SEQ ID NO: 1, the specification discloses and the claims recite probes that hybridize preferentially to the DNA (SEQ ID NO: 1) of human MiRP1 and four human MiRP1 nucleotide sequences mutated at a single amino acid, a) Q9E-hMiRP1, b) M54T-hMiRP1, c) I57T-hMiRP1, or d) T8A-hMiRP1 (page 73), but not to any other nucleic acid sequence. However, the state of the prior art as exemplified by Wallace et al and Sambrook is such that determining the specificity of hybridization probes is empirical by nature and the effect of mismatches within an oligonucleotide probe is unpredictable. Furthermore, the as-filed specification does not provide sufficient guidance to determine the structural and functional limitation of a nucleic acid probe which hybridizes specifically to the DNA of claim 2 under any stringent condition wherein said stringent hybridization condition prevents said nucleic acid probe from hybridizing to DNA of SEQ ID NO: 1 and/or any allelic specific probe or primer which hybridizes to the DNA of claim 1 or an allelic variant thereof under any stringent condition. The lack of working examples in view of the prior art would result in an undue amount of experimentation for one skilled in the art to reasonably correlate probes composed of a 10mer fragment of SEQ ID NO: 1 to any other DNA probe that would meet the functional and structural limitations of the claimed embodiment. There are no suggestions as to what the target

sites in SEQ ID NO: 1 are or what modifications can be made while retaining the functional limitation. In addition, dependent claims 6 and 7 are the only claims to recite limitations on the nucleic acid (*e.g.* probe of claim 5 that 10-100 bases long; probe of claim 6 that **comprises** at least ten contiguous bases from SEQ ID NO: 1 or the complement of thereof). Since the nucleotide sequence mentioned merely **comprises** at least ten contiguous nucleotides from a nucleotide sequence selected from SEQ ID NO: 1, it encompasses any random sequence of any length as long as it has a stretch of at least ten contiguous nucleotides that is the same as SEQ ID 1. Furthermore, since there is no limitation that the claimed nucleic acid be complementary to the nucleotide sequence at the stretch of at least ten contiguous nucleotides that is the same as SEQ ID NO: 1, the structural limitations encompass any nucleic acid consisting of 10 to 100 bases long. Thus, claim 6 encompasses any nucleic acid consisting of 10 to 100 in length and hybridizes to DNA of SEQ ID NO: 1. Since the structural limitations of the claim clearly covers any nucleic acid that is 10 to 100 nucleotides in length and in view of the unpredictable nature of the art and lack of guidance with respect to appropriate modifications, one skilled in the art would have to make and test with further experimentation an enormous number of nucleic acids that meet the structural limitations to determine which probes also meet the functional limitation. This amount of experimentation would result in undue experimentation for one skilled in the art. Therefore, based on the unpredictable nature of the invention and the state of the prior art, the limited guidance and working examples in the as-filed specification, and the extensive quantity of experimentation needed to identify the nucleic acids encompassed by the claims, it would require an undue amount of experimentation to identify or make the nucleic acids encompassed by the claims (*e.g.* a nucleic acid probe which hybridizes specifically to the DNA of claim 2

under stringent conditions wherein said stringent hybridization conditions prevent said nucleic acid probe from hybridizing to DNA of SEQ ID NO: 1) other than an isolated nucleic acid comprising of at least 10 nucleotides which hybridizes DNA of SEQ ID NO: 1. Furthermore, with respect to the claimed embodiment encompassing the use of any primer which hybridizes to the DNA encoding mutated polypeptide of SEQ ID NO: 2, it is not apparent to one skilled in the art in view of the concerns listed above encompassing probes how to make and/or use amino acid primers encoding any fragment of SEQ ID NO: 2. First, DNA is required for amplification of any DNA sequence. One skilled in the art would understand that several conditions for producing primers from oligonucleotides, typically 15-30 bases long, would need an undue amount of experimentation to determine what region of interest in the unknown amino acid sequence would not contain bases complementary to themselves or with each other. Thus, the disclosure is not enabled for any primer, which would amplify any isolated DNA sequence encoding SEQ ID NO: 1 using an amino acid sequence. In addition, the as-filed specification is not enabled for any amino acid primer that is used to amplify any fragment of the amino acid sequence set forth in SEQ ID NO: 2.

Also, the disclosure does not provide sufficient guidance for performing a single base extension (SBE) across a polymorphic site, since a polymorphic site is not described in such a way that one skilled in the art would be able to perform the SBE without undue experimentation. The state of art defines a polymorphism "as a locus in which two or more alleles have gene frequencies greater than 0.01 (1%) in a population (Jorde et al., Medical Genetics, 2nd ed., Mosby, 1999, page 328)." "When this criterion is not fulfilled the locus is monomorphic (Jorde et al., page 328)." The applicants display four mutations in the human MiRP1 gene associated

with arrhythmia (pages 72-73). However, in view of the definition of a polymorphism, the mutations do not reasonably correlate to a polymorphism and/or any other polymorphic site in the human MiRP1 gene. Furthermore, in view of the state of the art for producing primers, the as-filed specification does not provide sufficient guidance for what is the starting material required for use in a method of amplifying an exon of KCNE2 or allelic variant thereof wherein said method comprises using a pair of primers.

With respect to the claimed invention reading on an isolated DNA comprising a nucleic acid sequence encoding for human MiRP1 set forth SEQ ID NO: 2 and its uses. Claims 25, 26, 29, and 30 read on an in vivo cell transfected with a vector comprising a nucleic acid sequence encoding a polypeptide in SEQ ID NO: 2 or any fragment thereof. Furthermore, one skilled in the art would consider that they only use for transfecting a cell in vivo would be for use in a therapeutic method to treat a mammal. Therefore, claims 25, 26, 29, and 30 lie in the field of gene therapy.

With respect to claims directed to compositions useful for gene therapy and directed to any therapeutic treatments of a mammal; the state of the art in 1998, exemplified Anderson et al., *Nature*, Vol. 392, pp. 25-30, April 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method (Anderson, *Nature*, Vol. 392, pp. 25-30, April 1998).

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson indicates that the state of the art before 1998, and teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Thus, gene therapy is considered highly unpredictable.

The as-filed specification contemplates a method of supplying a wild-type KCNE2 to a cell, which carries a mutant KCNE2 allele (pages 52-55). In addition, the specification contemplates using KCNE2 gene or fragment in a method of gene therapy in order to increase the amount of the KCNE gene expressed in cells. The disclosure recites that gene transfer systems (*e.g.* viral, non-viral, defective viral vectors, replicant viral vectors) known in the art may be useful in the practice of gene therapy methods of the present invention. The specification also contemplates using a retroviral vector producer cell line to produce a therapeutic response and that the injection of producer cells would then provide a continuous source of vector particles. Furthermore, the specification contemplates that if the transfected gene is not permanently incorporated into the genome of each targeted cell, the treatment may have to be repeated periodically.

In addition to the doubts expressed by Verma and Anderson, the state of the art for using vectors for gene therapy as exemplified by Mountain (*Trends Biotechnol.* Vol. 18, pp. 119-128, 2000). Mountain teaches:

> Gene transfer to somatic cells can take place in vivo or ex vivo (page 119, left column, 3rd paragraph). Ex vivo offers the advantage of more-efficient gene transfer and the possibility of cell propagation to generate higher cell doses (page 119). However, it the notable disadvantages of being largely patient-specific as a result of cell immunogenicity (page 119). In vivo methods used several types of vectors (*e.g.* viral, non-viral, physical). The main disadvantage with viral vectors is insert-size limitation and immunogenicity (page 119, right column, 1st paragraph). Non-viral vectors give less efficient transfection especially in vivo) and more-transient expression (pages 119-120). Non-viral vectors

giving efficient gene transfer in vivo are not yet available (page 125, right column, 3rd paragraph). Mountain further states that "integrating vectors, and perhaps most non-integrating vectors, transgene expression appears to be limited and usually silenced by incorporation into condensed and transcriptionally inactive chromatin, both in vivo and ex vivo (page, 125, right column, 1st paragraph).

In view of the state of the art, the specification is not enabled for any method of gene therapy (ex vivo or in vivo). Since, it is known in the art that efficient delivery of therapeutic gene and appropriate gene expression is crucial issues for clinically relevant gene therapy. The specification does not provide sufficient guidance for one skilled in the art how to determine what amount of MiRP1 gene expression is needed for a therapeutic response in any mammal. In addition, gene therapy produces transient expression of the therapeutic gene, which requires additional treatment. This additional treatment, which the specification contemplates (page 54) results in an immune response in the mammal that results in unsuccessful expression of the therapeutic gene. Furthermore, the specification does not provide sufficient guidance for what would happen when the mammal that is deficient or null in the expression MiRP1 is exposed to viral antigens, potential viral recombination, or an immunogenic novel protein (MiRP1). The disclosure does not provide sufficient guidance for how to circumvent the immune response in any mammal undergoing a method of gene therapy using MiRP1 (nucleotide sequence encoding SEQ ID NO: 2) transfected in a vector and/or a genetically modified cell. Thus, in view of the state of the art the specification does not provide sufficient guidance for what vectors could be used to produce a therapeutic response using any vector encoding the nucleotide sequence encoding MiRP1 (SEQ ID NO: 2).

At best, the application and the state of the art only provide sufficient guidance for enabling claims directed to 1) a nucleic acid comprising a nucleotide sequence coding for human MiRP1 set forth in SEQ ID NO: 2 or the complement of SEQ ID NO: 1; 2) An in vitro cell transfected with the DNA of SEQ ID NO: 2; 3) A vector comprising the isolated DNA of SEQ ID NO: 2; 4) An in vitro cell transfected with the vector of 4; 5) An isolated nucleic acid comprising of at least 10 consecutive nucleotide residues of SEQ ID NO: 1 6) An isolated nucleic acid consisting of a mutated human MiRP1 (SEQ ID NO:1) selected from the group consisting of one of the following mutant human MiRP1 genes: a) Q9E-hMiRP1, b) M54T-hMiRP1, c) I57T-hMiRP1, or d) T8A-hMiRP1.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable 1-6, listed above. One would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the application's disclosure, the unpredictability of gene therapy (Anderson, *Nature*, Vol. 392, pp.25-30, 1998) and developing effective vectors (Mountain, *Trends Biotechnol*, Vol. 18, pp. 119-128, 2000) for use in any method of gene therapy for LQT. In addition, the lack of guidance for using amino acid sequences as primers does not reasonably extrapolate to the full scope of the claimed invention encompassing the use of primers for amplifying any unknown DNA molecule encoding a mutated polypeptide of SEQ ID NO: 2 or amino acid sequence set forth in SEQ ID NO: 2. Furthermore, the disclosure does not provide sufficient guidance in view of Chiu et al., *Folding and Design*, 1998, pp. 23-228 and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991) for making

and/or using probes that hybridize to unknown DNA sequences encoding a mutated polypeptide of SEQ ID NO: 2.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 2, 3, 4, 5, and 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "hybridizes under stringent conditions" in claims 1, 3, 4, and 5 is a relative phrase, which renders the claim indefinite. The phrase "hybridizes under stringent conditions" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The definition of the phrase "hybridizes under stringent conditions" is not a closed definition from reading page 36 in the as-filed specification. The parameters of what constitutes moderately or highly stringent conditions are not defined by the claims.

The term "herein" in claim 2 is a relative term, which renders the claim indefinite. The term "herein" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification or claims do not define the metes and bounds of an isolated DNA encoding a polypeptide of SEQ ID NO: 2 comprising a mutation disclosed herein.

Claims 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP

§ 2172.01. The omitted elements are: polynucleotide sequence encoding the polypeptide of SEQ ID NO: 2 or allelic variant thereof. The specification and claims do not describe the metes and bounds of primers that hybridize to a polypeptide sequence set forth in SEQ ID NO: 2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, as best understood, read on any nucleotide sequence comprising a 1%-99% identity to a nucleotide sequence encoding SEQ ID NO: 2, which could be a mutation of the nucleic acid sequence encoding the amino acid set forth in SEQ ID NO: 2.

Claims 1g, 5, 6, 7, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Kurtz et al (US Patent Nos. 5,620,892, 15 April 1997). Kurtz discloses a nucleotide sequence for human minK with 85 percent similarity that would hybridize to **applicants' nucleotide sequence encoding the amino acid set forth in SEQ ID NO: 2** (column 2, lines 55-61, SEQ ID NO: 5). In addition, Kurtz teaches that oligonucleotides were used to produce portions of the TRK2 coding region (Fig.4, SEQ ID NO: 5) corresponding to the 5' (600bp) and 3' (800bp) ends of the coding region by polymerase chain reaction amplification of yeast genomic DNA (column 5, lines 10-14). Furthermore, Kurtz claims a modified cell, wherein the minK protein has the amino acid sequence encoded by a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 5 (column 39, lines 36-38).

Claims 1(g, h), 2, 5, 6, 25, 26, 27, 28, 29, and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg (NCI-CGAP, http://www.ncbi.nlm.nih.gov/ncicgap, AI339609). Strausberg teaches a MINK Human slow voltage-gated potassium channel cDNA sequence with 99.1 percent similarity to the applicants' nucleic sequence encoding the amino acid sequence set forth in SEQ ID NO: 2. Furthermore, Strausberg transfected a vector consisting of the sequence into cells to produce the cDNA. In addition, the nucleic acid encoding the applicant's amino acid sequence set forth in SEQ ID NO: 2 would hybridize to the cDNA sequence set forth by Strausberg. As evidence to the contrary, the cDNA sequence taught by Strausberg displays all properties encompass in the claimed invention.

Claims 1(a, g, h), 2, 5, 6, 25, 26, 27, 28, 29, and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg (NCI-CGAP, http://www.ncbi.nlm.nih.gov/ncicgap, AI246239). Strausberg teaches a MINK Human slow voltage-gated potassium channel cDNA sequence with 100 percent similarity to the applicants' nucleic sequence encoding the amino acid sequence set forth in SEQ ID NO: 2 and vectors encoding the cDNA, and in vitro cells comprising the cDNA. Furthermore, Strausberg transfected a vector consisting of the sequence into cells to produce the cDNA. In addition, the nucleic acid encoding the applicant's amino acid sequence set forth in SEQ ID NO: 2 would hybridize to the cDNA sequence set forth by Strausberg. As evidence to the contrary, the cDNA sequence taught by Strausberg displays all properties encompass in the claimed invention.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Tracey Johnson whose telephone number is (703) 305-2982.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on M-F, (730-400 EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached at (703) 305-4051.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1633
August 24, 2001

DAVE T. NGUYEN
PRIMARY EXAMINER